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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/050,665	01/16/2002	Jyh-Lyh Juang	13217-002001	6059

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EXAMINER	
GUZO, DAVID	

ART UNIT	PAPER NUMBER
1636	13

DATE MAILED: 10/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application N .	Applicant(s)	
	10/050,665	JUANG ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 March 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because:
> It does not identify the mailing address of each inventor. A mailing address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing address should include the ZIP Code designation. The mailing address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.
> Specifically, the post office address for inventor Dung-Fang Lee is not identified.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8, 10, 14-22, 24-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Miller.

Applicants claim a recombinant virus (which can be a baculovirus) capable of infecting a non-permissive cell, comprising a first nucleic acid encoding a detectable marker operably linked to a first promoter (which can be a polyhedrin promoter), wherein said first promoter is active in a host cell and inactive in a non-permissive cell (which can be a non-permissive insect cell such as a *Drosophila* cell or mammalian or human cell) and a second nucleic acid which includes an exogenous nucleic acid sequence operably linked to a second promoter (which can be a RSV promoter),

wherein said second promoter is active in the non-permissive cell. Applicants claim a method for selecting a viral plaque for infection of non-permissive cells, comprising providing the aforementioned recombinant virus, infecting a host cell culture with said virus and identifying a viral plaque by detecting expression of the detectable marker, thereby selecting a viral plaque for infection of non-permissive cells. Applicants also claim a method for producing a protein in a non-permissive cell *in vitro* or *in vivo*, comprising providing the aforementioned recombinant virus, infecting a host cell culture with the virus, selecting a viral plaque by identifying expression of the detectable marker, amplifying the virus from the plaque and infecting a non-permissive host cell with the virus. It is noted that applicants define a selectable marker as any reporter molecule that is detectable.

Miller et al. (Cited by applicants, U.S. Patent 5,004,687, issued 04/02/97, see whole document, particularly the paragraph bridging columns 5-6; the paragraph bridging columns 6-7, columns 8-9, lines 39-66 and Examples I-IV) recites a recombinant baculovirus capable of infecting a non-permissive host cell (such as a *Drosophila* cell or a mammalian cell) comprising a first nucleic acid encoding a detectable marker (B-galactosidase) operably linked to a first promoter (polyhedrin promoter) active in host cells and inactive in non-permissive cells such as mammalian cells or non-permissive insect cells (such as *Drosophila* cells) and a second nucleic acid which includes an exogenous nucleic acid sequence operably linked to a second promoter (which can be the RSV-LTR promoter) wherein said promoter is active in non-permissive cells such as mammalian and human cells as well as non-permissive insect

cells. Miller also teaches a method for selecting a viral plaque for infection of non-permissive cells, comprising providing the aforementioned baculovirus, infecting a host cell culture with the virus and identifying a viral plaque by detecting expression of the detectable marker, thereby selecting a plaque for infection of non-permissive cells. Miller also recites a method for expression of a protein of interest in a non-permissive cell (the cell can be *in vitro* or *in vivo* in a insect host so as to expand host range of a given baculovirus), comprising infecting a host cell culture with the aforementioned virus, selecting a viral plaque by identifying expression of the detectable marker, amplifying the virus by further culture of the virus originating from the selected plaque and infecting a non-permissive host cell with the virus. Miller therefore teaches the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless--
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 8-9 and 12-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Novy et al.

Applicants' invention is as described above. Applicants also claim a recombinant virus wherein the first promoter is a p10 promoter or wherein the detectable marker in

the virus is a sequence encoding a fluorescent protein such as green fluorescent protein (GFP).

Novy et al. (U.S. Patent 6,589,783, issued 07/08/03, filed 04/13/00, see whole document, particularly Fig. 1; column 1, lines 36-46; column 4, lines 22-41; the paragraphs bridging columns 5-6 and 6-7; column 6, lines 6-24 and Claims 1-9) recites a recombinant baculovirus (vTriEx-1) capable of infecting a non-permissive host cell comprising a first nucleic acid comprising a first promoter (which can be p10 or polyhedrin) operably linked to a detectable marker (such as GFP) which is active in a host cell (insect cell) and is not active in a non-permissive host cell (mammalian or bacterial cell) and a second nucleic acid sequence which includes an exogenous nucleic acid sequence operably linked to a second promoter (T7 lac promoter or chicken β-actin promoter) which is active in said non-permissive host cell (which can be a bacterium or a mammalian or human cell). Novy et al. therefore teaches the claimed invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 8-9, 12-14, 16-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim a genus of recombinant viruses capable of infecting any non-permissive cell comprising first and second promoters, wherein the first promoter is active in a host cell and the second promoter is active in a non-permissive cell. Applicants also claim methods of selecting a viral plaque for infection of non-permissive cells and a method of making a protein in a non-permissive cell comprising infecting non-permissive cells with the virus. Applicants provide examples of the claimed invention using baculoviruses.

The written description requirement for a claimed genus may be satisfied through **sufficient description of a representative number of species** by reduction to practice, disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties coupled with a known or disclosed correlation between function and structure or by a combination of such identifying characteristics sufficient to show applicant was in possession of the claimed genus. In the instant application, applicants provide no disclosure, other than for baculoviruses, on the generation of any recombinant viruses with the recited characteristics. Applicants recite the claimed recombinant viruses by function only without a correlation between structure and function. Applicants provide no guidance on which viruses would be suitable for the recited manipulations, no guidance on how the claimed recombinant viruses would be generated, no guidance on the specific promoter combinations used for any given virus - host cell combinations, etc. Applicants provide no teachings on any correlation

between the structure of the instant baculovirus examples and the structures of any other viruses (such as coronaviruses, papillomaviruses, alphaviruses, lentiviruses, etc.) with the instantly claimed characteristics. Given the broad scope of the claimed invention (reading on any recombinant virus capable of infecting any non-permissive cell), the lack of teachings on the generation of any recombinant viruses (with the exception of baculoviruses) and the lack of any correlation between the structure of the instantly recited baculoviruses and the structure of any of the other viruses encompassed within the claims, it must be considered that the one species disclosed by applicants (baculovirus) would not, in the view of the skilled artisan, be a representative number of species sufficient to describe the instant invention. It is noted that claims 16-21 are included in this rejection because the claims are not limited to baculoviruses, even though they are dependent on a claim which is limited to baculoviruses (See the objection under 37 CFR 1.75(c) to claims 16-21 recited below).

Claims 1, 8-9, 12-14 and 16-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for recombinant baculoviruses, a method of selecting baculoviral plaques for infection of non-permissive cells and methods of using said baculoviruses to express proteins in non-permissive cells, does not reasonably provide enablement for generating any recombinant viruses capable of expressing proteins in non-permissive cells or methods of selecting viral plaques for infection of non-permissive cells. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants' invention is as described in the above 35 USC 112, 1st paragraph (written description) rejection of claims 1, 8-9, 12-14 and 16-23.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor, but rather is a conclusion reaches by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

1) Unpredictability of the art. The art with regard to generating recombinant viruses capable of "infecting" non-permissive host cells is unpredictable. It must be considered that the ability of any given promoter to express a given gene in a cell which is non-permissive for any given virus, in the context of infection of the cells with said recombinant virus, must be determined on an empirical basis. It is unclear how a single promoter operably linked to an exogenous sequence of interest incorporated into a virus such as a retrovirus or coronavirus, etc. can result in the virus being capable of infecting a cell which is normally non-permissive for infection by the virus.

2) State of the art. The state of the art with regard to generation and use of recombinant viruses genetically engineered to be capable of infecting non-permissive

cells is poorly developed. Applicants present no teachings of the prior art on this subject.

3) Number of working examples. Applicants present no working examples of the claimed invention using non-baculoviruses.

4) Amount of guidance provided by applicants. Applicants provide no guidance on practicing the claimed invention with any viruses other than baculoviruses.

5) Scope of the invention. The scope of the invention is broad and encompasses any recombinant virus capable of infecting any non-permissive host cells and using said viruses to express proteins of interest in said host cells.

6) Nature of the invention. The invention involves complex areas of molecular biology involving changing the ability of a virus to infect cells normally non-permissive for virus infection.

7) Level of skill in the art. The level of skill in the art is high; however, given the absence of teachings on generation of recombinant viruses (other than baculoviruses) with the recited characteristics, the unpredictability of the art, the lack of working examples and the broad scope of the claimed invention, it must be considered that the skilled artisan would have needed to have conducted trial and error experimentation in order to attempt to practice the claimed invention.

Given the above analysis of the factors that the courts have determined are critical in ascertaining whether a claimed invention is enabled, it must be considered, absent evidence to the contrary, that the skilled artisan would have had to have

conducted undue and excessive experimentation in order to reduce to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (and dependent claims) are vague in the recitation of the phrase "capable of infecting a non-permissive cell" because it is unclear what "infecting" here means. The specification teaches generation of a recombinant baculovirus which is capable of expressing an exogenous protein of interest in non-permissive cells and not capable of replicating in the non-permissive cell. It is unclear if applicants mean the word "infecting" to be synonymous with expressing an exogenous protein in the non-permissive cell. Claim 1 is also vague in the recitation of the phrase "promoter is active in a host cell" because it is unclear what "host cell" applicants are referring to, i.e. a host cell permissive for replication of the virus?

Claim 13 is vague because applicants recite acronyms without a definition of the acronyms. Applicants need to spell out the names of the proteins followed by the acronym.

Claim 14 (and dependent claims) are vague because there is no antecedent basis for the term "the recombinant baculovirus" in the claim.

Claim 22 (and dependent claims) are unclear in the recitation of the phrase "amplifying the virus" because it is unclear if the is term refers to some amplification of the viral DNA (i.e. by use of a PCR method?) or growing the virus to generate a viral stock, etc.

Claims 16-21 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 16-21 depend ultimately from claim 15, claim 15 is limited to **a recombinant baculovirus**. However, claims 16-21 are broader than the claim from which they depend because they recite **any recombinant virus** and are not limited to a recombinant baculovirus.

Miscellaneous: Applicants' submission of Substitute Drawings on 03/15/02 is acknowledged. The Drawings can be substituted for the erroneously filed original drawings.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (703)

308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DAVID GUZO
PRIMARY EXAMINER

David Guzo
October 27, 2003